Malaysian Journal of Chemistry, 2020, Vol. 22(2), 69-81

Synthesis of Polyethanolamine Dendrons Using an Improved Reduction Method

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This work describes the synthesis of ethanolamine-based dendrons via an improved reduction method using potassium borohydride (KBH_4) and Raney nickel (Raney Ni). The synthesis constituted two iterative processes of Michael addition and nitrile reduction. Polyethanolamine dendrons (PEaDron) of up to Generation 2.0 were synthesised under optimised reaction conditions at atmospheric pressure and 40°C, with water as solvent, KBH_4:Raney Ni as catalyst at a ratio of 4:1, 1 h of stirring, and direct slow heating during isolation. The core remained as hydroxyl, whereas the amine group grew divergently. System efficacy was confirmed and fully characterised by IR, NMR, and MALDI-TOF spectroscopy analyses. The PEaDron featured a convenient centre for various reactions while the improved reduction method has the potential for the reduction of other nitrile compounds.

Key words: Dendron; nitrile reduction; Raney nickel; synthesis; characterisation

Received: October 2019; Accepted: April 2020

Dendron is a unique macromolecule because it possesses two functional groups, namely the core and periphery [1-6]. By contrast, dendrimers are composed of multifunctional core units, organised repetitive units, and a definite number of peripheral branching units made of different terminal moieties [5-10]. All parts of dendrons and dendrimers are indispensable because the existence of a micro-environment in the core units, which is contributed by the redox active centre, determines encapsulation selectivity [11, 12]. Moreover, the cavities between the layers of different generations provide containment sites [5, 13, 14] and densely packed active termini sites for various chemical reactions [12]. These characteristics make them undeniably crucial in biomedical research [9, 15-20], nanotechnology [13], sensors and detectors [7, 21], biotechnology [15, 22-24], and catalyst support [3, 13].

Comparisons of dendrons and dendrimers are highly important because dendrimers comprise of dendrons, but dendrons can also function independently. An open question is how dendrons contribute to the progression of synthesis and application of macromolecules. One of the current trends is to construct dendrimers with modified dendrons by wedging [2, 5, 25-27] and assembling them into globular dendrimers [9, 22]. A previous report has demonstrated such synthesis with the use of dendrons, such as poly(amidoamine) (PAMAM) dendrons, with the poly(propylene oxide) dendron acting as the amphiphilic co-polymer for drug encapsulation and release [28]. Other studies reported the synthesis of gold nanoparticles utilising carbosilane dendrons as stabiliser [3] and monomers of arylalkyl ether at different generations, which perceived different capsizes of electroactive species [11, 29].

Several authors have regarded dendrons to have grafting potentials. In 1984, Tomalia et al. was one of the first to synthesise a dendronised polymer by grafting a poly(ethyleneimine) dendron on polymer [30]. Their work has since resulted in mass research on this field. Maraval et al. demonstrated the instant construction of high-generation dendrimers by manipulating monomers, as in ‘Lego’ chemistry [1]. This utilisation lessened tedious multistep procedures, thereby making dendrimer synthesis easy.

Gao and Yan evaluated monomers in the field of hyperbranched polymers and macromolecules [31] and categorised them into single and double monomer methodologies. According to them, AB_n monomers with different generations or functional group moieties are potential grafters in linear-dendritic hybrids, dendrigrafts or dendronised polymers, hyperbranched polymers [32, 33], multi-arm star polymers [34], and hypergrafts or hypergrafted polymers [35].

Dendrons are usually built in generations divergently, and the approach begins from the focal point growing outwards, forming wedges and grafts via convergence [2, 3, 36]. Compared with dendrimers, dendrons have the advantage of dual functionality with a focal point for exploitation. Different types of focal points, such as phenolic [37], carboxylic [38], glycinylurea [39], dipeptidyl core [40], metal core [6, 12, 41], and hydroxyl focal points [42, 43], have been discovered. Although many types of focal points and origin cores have been discovered, only a few mentioned the renowned hydroxyl (OH) group, which displays low non-specific binding and high aqueous solubility. With this focal point, dendrimer construction via convergence can proceed inwards, leading to the final attachment of the dendron to the core.

The OH functional group reacts in many chemical reactions, such as esterification [10, 14, 19], metal sorption [44], Michael addition [10, 18] and acrylation [45]. Similar works on dendrons demonstrated the building of dendrons using well-known dendrimers, such as polyamidoamine (PAMAM) [27, 46], poly(etherimine) (PEI) [47] and poly(propyleneimine) (PPI) [37, 48]. Even though the above-mentioned dendrons look similar, the difference in functional groups in the branching unit may lead to different chemical properties. Furthermore, primary amine was selected as the terminal group as it is vastly employed in a range of chemical reactions.

With the myriad of possible applications of a single dendron, this work presents the synthesis of dendron based on water-soluble poly(ethanolamine) dendron (PEaDron) using an improved reduction method. Synthesis begins with an iterative addition method on the surface unit via Michael addition and nitrile reduction. Through convergence, it starts with ethanolamine (ENA) as the core and hydroxyl as the focal point and increasing units of amine group (NH_2) with each tier generation. Building numerous dendrimers is time consuming [49]; therefore, an efficient PEaDron synthesis method with improved reduction is necessary. Nitrile reduction is critical in most dendrimer synthesis processes because it is a synthon for amine formation. Table 1 shows types of nitrile reduction methods with a Raney Ni system; however, none of previously reported works utilised water as solvent with the presence of commercialised Raney nickel and hydrogen donor by KBH_4. This work describes the synthesis of PEaDrons of up to Generation 2.0 using ENA as base and Raney Ni as catalyst, with water as solvent.

EXPERIMENTAL SECTION

Chemicals and Reagents

All chemicals used were of analytical reagent grade unless otherwise stated. ENA, KBH_4, NaOH, acrylonitrile, acetone, absolute ethanol, methanol, DMSO, and THF were obtained from Merck (Darmstadt, Germany), whereas *n*-hexane, ethyl acetate, chloroform, toluene, and 96% ethanol were purchased from QRec (New Zealand). Raney Ni was used as reduction catalyst and ordered from Nacalai Tesque (Kyoto, Japan).

Instruments

The synthesised materials were characterised using Perkin Elmer Spectrum One Fourier-transform infrared (FTIR) spectroscopy. Each analysis was performed with 10 scans, deducting the background spectrum beforehand. Various peaks confirmed the presence of different functional groups. Results were run with KBr pellet- and nujol oil-coated film. The proton and carbon (^{1}H-NMR and ^{13}C-NMR, respectively) MHz nuclear magnetic resonance (NMR) spectra were confirmed with NMR Bruker DPX-400 using NMR solvent and deuterium oxide (D_2O) to dilute PEaDron of different generations. The following abbreviations are used to explain the multiplicities: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad.

Table 1. Types of nitrile reduction method with Raney Ni.

No	Method	Isolated yield %	Reference
1.	Raney Ni (Anode) + NaOH (Cathode) + $NaBH_4$ (Electrolysis)	72	[50]
2.	Raney Ni + palladium on charcoal + 1,4-dioxane/water (4:1) + lithium hydroxide monohydrate + hydrogen atmosphere (45 psi) + Room Temperature (rt)	86	[51]
3.	Raney Ni + KBH_4 + dry ethanol at mild temperature (45 mins)	80	[52]
4.	Raney Ni + ethanol + 3.0 MPa H_2 pressure + 110ºC	<40	[53]
5.	Raney Ni + hydrazinium monoformate + nitrile + methanol + nitrogen atmosphere.	81	[54]
6.	Raney Ni + KBH_4 + H_2O+ 40ºC	90	This work

Synthesis of Dendrons

Activation of Raney Ni

Firstly, 1.4 g of nickel–aluminium alloy (50–50 Ni/Al wt.%) was gradually sprinkled into 5 mL of NaOH (6 mol/L) at 50°C. The reaction was continuously stirred for 3 h. About 5 mL of NaOH was poured into the mixture every hour, and the mixture was continuously stirred at 6/10 speed. Raney Ni was then washed with dry absolute ethanol and deionised water alternately for five times each in a centrifuge. The rate of spinning was set at 35/40 rpm at 5 min each. Once activated, the sample was kept in absolute ethanol in a tight-sealed container.

Synthesis of PEaDron G0.5

Ethanolamine (12.04 cm^3, 0.2 mol) was added to 80 mL of oxygen-free distilled water in a 0.5 L round-bottomed flask. Acrylonitrile (27.4 cm^3, 0.42 mol) was added at 80°C, and the system was vigorously stirred for 1 h. Toluene–methanol (9:1 v/v ratio) was added into the system and shaken forcefully to remove excess acrylonitrile. When two layers formed, the lower one was collected, and the upper one was decanted. The yellow liquid was heated on a hot plate at low heat (80°C) until all water evaporated. Light yellow oil was obtained (95% yield). Fig. 2 shows the FTIR results. FTIR λ_{max} (nujol): v (cm^{-1}): 3360–3500 (hydroxyl), 2945,2857 (C–H stretching), 2248 (nitrile), 1650 (N–H deflection of amine), 1456 (C–H bend), 1423(C–N bend) and 1367,1277 (C–N stretch). ^{1}H-NMR (MeOD, 400 MHz): δ (ppm) = 3.65(^{a}t, 2H), 2.74 (^{b}t, 2H), 2.94 (^{c}t, 4H), 2.62 (^{d}t, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 120.1, 68.9, 65.44, 60.2, 59.0, 56.8, 54.4, 52.2, 49.5, 43.7, 18.3, 17.3, 15.7. The results were consistent with the functional group in Fig. 3.

Synthesis of PEaDron G1.0

Approximately 27.8 mL of PEaDron G0.5 (0.2 mol) was added to 40 mL of oxygen-free distilled water in a 250 mL beaker and stirred until the temperature rose to 40°C. KBH_4 (2.16 g, 0.04 mol) was added, followed by 0.64 g of the moisture weight of Raney Ni (0.64 g, 0.01 mol). The system was covered with parafilm throughout 1 h of stirring. Raney Ni was removed via centrifugation. The yellow liquid was heated on a hot plate at low heat (80°C) until a sticky white solid formed. DMSO was added to the solid to wash away KBH_4 under high-speed magnetic stirring. The washing steps were repeated three times. Fine white solid was collected, heated in an oven to remove moisture, and kept in a tight-sealed container (90% yield). FTIR λ_{max} (KBr): v (cm^{-1}): 3405 (O-H), 1645 (N–H deflection of amine), 1471 (C–H bend), 1421(C–N bend) and 1372 (C–N stretch). ^{1}H-NMR (MeOD, 400 MHz): δ (ppm) = 2.42–2.85 (^{e}m, 12H), 3.72 (^{f}m, 4H).

Synthesis of PEaDron G1.5

PEaDRon G1.0 (1.47 g, 0.01 mol) was added to 40 mL of oxygen-free distilled water in a 0.5 L round-bottomed flask. Acrylonitrile (27.4 cm^3, 0.42 mol) was added at 80°C, and the system was vigorously stirred for 12 h. Toluene–methanol (9:1 v/v ratio) was added to remove excess acrylonitrile. For liquid–liquid separation, the lower portion was collected after the bubbles had settled. The yellow liquid was heated on a hot plate at low heat (80°C) in a 50 mL beaker until a sticky yellow solid was observed. The light yellow oil on top of the solid was then collected. Once cooled, a sticky yellow semisolid formed (75% yield). FTIR λmax -(KBr): v (cm^{-1}): 3363 (O-H), 2962,2847 (C–H stretching), 2251 (C≡N), 1668 (N–H deflection of amine), 1446 (C–H bend) and 1377 (C–N stretch). ^{1}H-NMR (MeOD, 400 MHz): δ (ppm) = 3.82 (^{g}t, 2H), 3.78–3.65 (^{h,i}m, 10H), 2.51–2.30 (^{j}br,m, 12H), 2.94–2.60 (^{k}m, 8H).^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 129.5, 128.5, 119.8, 67.8, 57.9, 45.0, 37.6, 35.4, 20.7, 18.1.

Synthesis of PEaDron G2.0

Approximately 3.03 g of PEaDron G0.5 (0.01 mol) was added to 40 mL of oxygen-free distilled water in a 100 mL beaker and stirred until the temperature rose to 40°C. KBH_4 (2.16 g, 0.04 mol) was added, followed by 0.64 g of the moisture weight of Raney Ni (0.64 g, 0.01 mol). The system was covered with parafilm throughout 2 h of stirring. Raney Ni was removed by centrifugation. The yellow liquid was heated on a hot plate at low heat (80°C). Once water evaporated, DMSO was added to wash away KBH_4 under high-speed magnetic stirring. The washing steps were repeated three times. Fine white solid was collected and heated in an oven to remove moisture. The solid was kept in a tight-sealed container (80% yield). FTIR λ_{max} (KBr): v (cm^{-1}): 3468 (O-H), 3362, 3296 (primary amine), 2927,2857 (C–H stretching), 1647 (N–H deflection of amine), 1484 (C–H bend), 1420(C–N bend) and 1376 (C–N stretch). ^{1}H-NMR (D_2O, 400 MHz): δ (ppm) = 3.61–3.7(^{l}m, 2H), 3.85–3.76 (^{m}m, 10H), 3.36–3.5 (^{n}m, 4H), 2.38–2.45 (^{o}m, 16H), 3.16 (^{p}m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 59.0, 40.1, 38.9.

Optimisation of Nitrile Reduction in PEaDron-CN

The keys for nitrile reduction lie on the catalyst with relevant solvent and conditions. Conditions, such as type of solvent, reaction time, temperature, amount of KBH_4, and drying system, were monitored for best reduction results (Table 2). Other reduction methods using cobalt(II) chloride–KBH_4 and hydrazine hydrate–Raney Ni were attempted, but poor results were yielded, and nitrile reduction was incomplete. Therefore, only Raney Ni–KBH_4 was further optimised because the method produced the highest yield among the reduction methods tested.

Table 2. Optimisation of condition for Nitrile Reduction in PEaDron-CN

Optimisation Condition	Raney Nickel + Potassium Borohydride (KBH_4)	Physical Appearance	Presence of nitrile peak in FTIR	Yield (%)
Solvent	Methanol	Clear yellow oil	Yes	-
	Ethanol	Clear yellow oil	Yes	-
	H_2O	Rough white solid	No	18
Reaction Time	PEaDron G1.0 – 1Hr	Rough white solid	No	18
	– 2Hr	Rough white solid	No	20
	PEaDron G2.0 – 1Hr	Sticky yellow solid	Yes	-
	– 2Hr	Sticky yellow solid	Yes	-
	– 6Hr	Sticky white solid	No	33
	– 12Hr	Rough white solid	No	31
	– 24Hr	Rough white solid	No	48
Reaction Temperature	Room temperature	Rough grey solid	No	48
	40°C	Fine white solid	No	75
	70°C	Sticky white solid	No	36
	80°C	Sticky white solid	No	33
KBH_4	Ratio to Raney Nickel			
	4:1	Coarse white solid	No	55
	8:1	Coarse white solid	No	52
	16:1	Coarse white solid	No	56
Drying System	Rotary Evaporator	Sticky yellow solid	No	15
	Rotary Evaporator + Vacuum	Sticky white solid	No	35
	Direct Heating (80°C)			
	Direct Heating (40°C)	Coarse white solid	No	56
		Fine white solid	No	90

RESULTS AND DISCUSSION

Synthesis of PEaDron

PEaDron was synthesised using ethanolamine as starting material. The synthetic routes for PEaDron G0.5 to G2.0 are outlined in Figure 1. Divergent synthesis started with a two-step preparation process. ENA was selected as the base with hydroxyl as the focal point to improve the solubility of its components. By contrast, the amine group acted as the branching point for generational growth. Figure 1 illustrates the synthesis of PEaDron G0.5 via Michael addition between acrylonitrile/water and ethanolamine and the reduction of the –CN bond using KBH_4 to obtain PEaDron generation 1.0. The repetition of the cycle resulted in the formation of two generations of PEaDron.

The solubility between the salts and products differed; therefore, simple separation steps could be adopted to isolate the products. At each reduction procedure, inorganic salts were removed by solubilising the material with DMSO, followed by filtration and drying under low heat. Washing continued until no more murky water was found, leading to high conversion % from nitrile to amine group and yield. The product formed in PEaDron G0.5 was a clear yellow liquid unlike the normal physical appearance of PPI dendrimers, which is solid white. It then emerged as a fine white solid at G1.0, a sticky yellow semisolid at G1.5, and a rough white solid at G2.0. Nevertheless, a yellow sticky semisolid at PEaDron G1.0 formed after being cooled from its previous state of yellow sticky oil.

Reduction Optimisation

Initially, the reduction of nitrile was attempted with pre-existing reduction methods, such as Co-Cl/$NaBH_4$/MeOH, Co-Cl/KBH_4/MeOH, Co-Cl /KBH_4/EtOH, Raney Ni/hydrazine hydrate/EtOH, Raney Ni/ KBH_4/EtOH, and Raney Ni/ KBH_4/MeOH at atmospheric pressure, but previous efforts were deemed unsuccessful. Water was used as solvent to overcome this setback, as it has better affinity with hydroxyl group compared to other solvents resulting in the desired dendron. It was observed that in this reduction system, MeOH/EtOH showed slower reaction compared to water and the current reduction method showed slight change in the reaction and no physical changes occurred for PEaDron G0.5. With dendrons G1.0 and G2.0 in hand, the next step was the optimisation of reduction conditions (solvent, reaction time, reaction temperature, ratio of KBH_4:Raney Ni, and drying system), as shown in Table 2. Thus, atmospheric pressure (40°C), water as solvent, catalyst ratio of 4:1 (KBH_4:Raney Ni), 1 h of stirring, and direct slow heating were found to be the optimal conditions for the synthesis of PEaDron G1.0. For G2.0, all conditions remained the same, except for the adjustment of stirring for up to 6 h. The purpose of direct heating was to remove the presence of solvent, water. Compared with high-temperature direct heating, slow heating improved the texture of the product, as in the fine white solid. Each reduction completion was verified with the disappearance of nitrile peak at 2250 cm^{-1} in IR spectroscopy. As a result of different approaches of reduction and optimisation, the correct alternative of reagents and reaction conditions were effective for PEaDron synthesis. The benefits of this synthetic procedure include simplicity and fast reaction, reaction at atmospheric pressure and water is used as solvent, thus more environmentally friendly. Besides, it offers high and qualitative yields, and can be prepared in bulk quantities thus potentially attractive for various reaction sequences at peripheries and focal points.

Structure Characterisation of PEaDron

FTIR

The synthesised PEaDron was confirmed from matching the peaks and functional groups in the FTIR and NMR spectra. The regular appearance of functional groups, such as the hydroxyl group, was observed

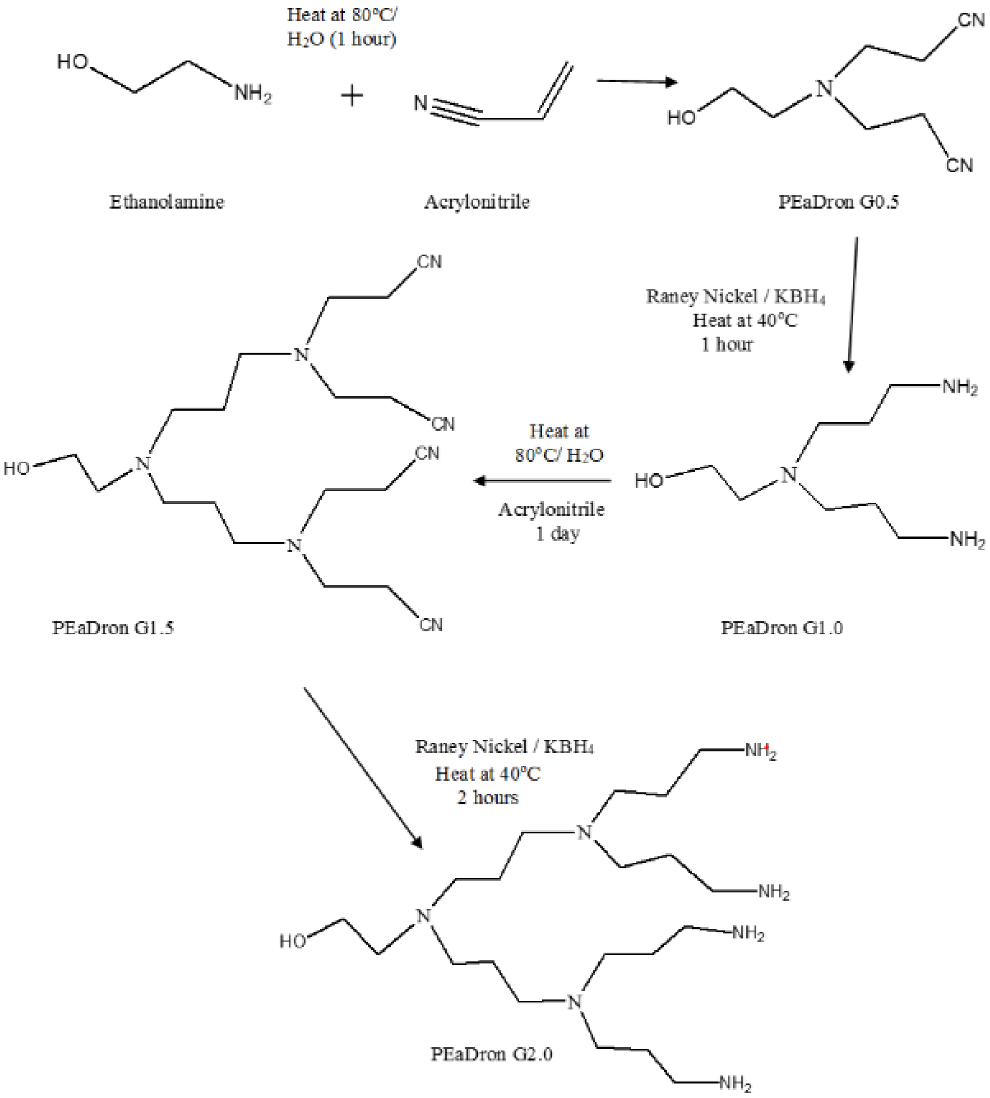


Figure 1. Synthesis outline of PEaDron Generation 0.5 to Generation 2.0.

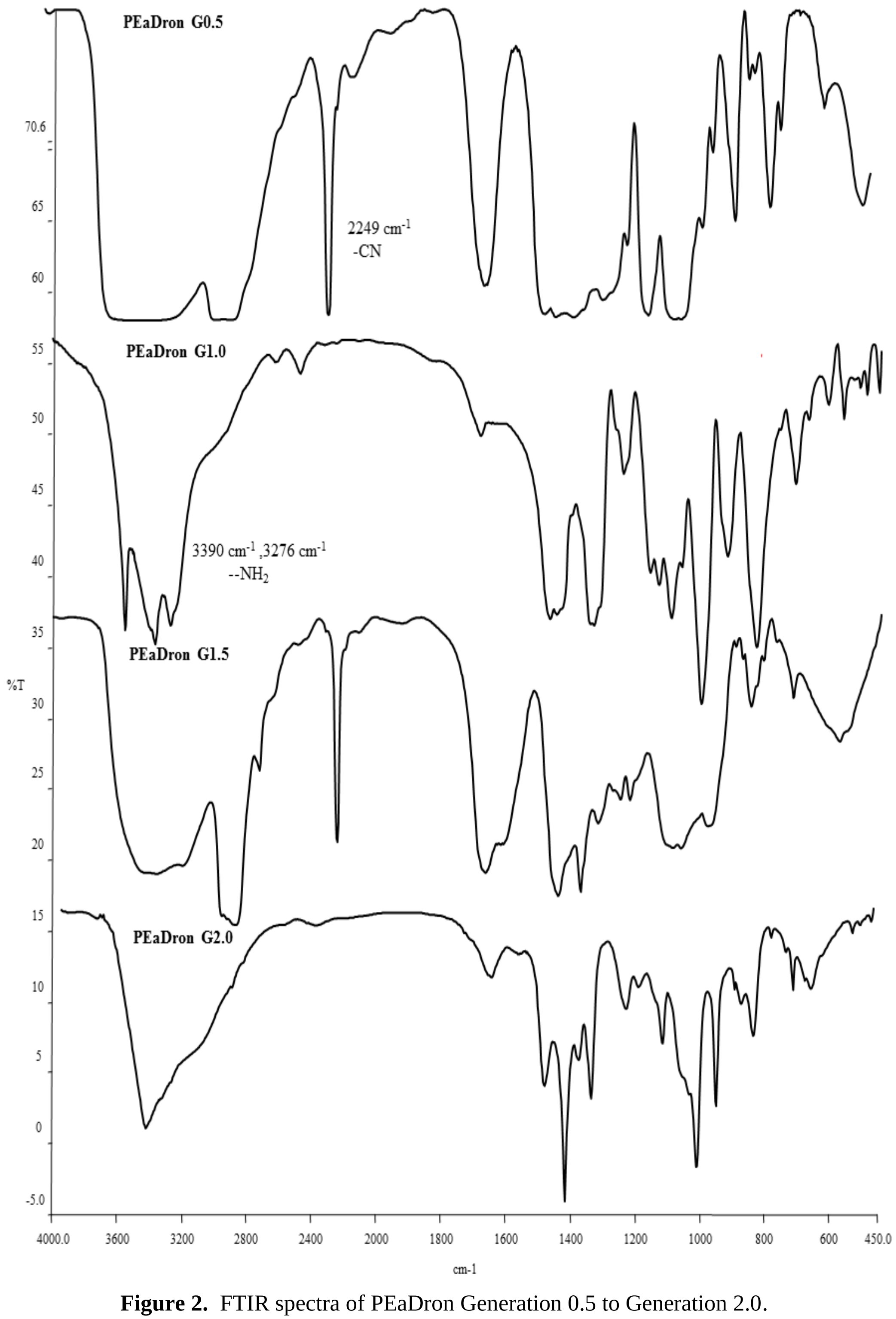


Figure 2. FTIR spectra of PEaDron Generation 0.5 to Generation 2.0.

throughout Generations 0.5 to 2.0, and the nitrile and amine groups appeared alternately at the peripheries. Therefore, by observing the spectral changes in IR, the reduction and formation of nitrile could be monitored. Figure 2 shows the assemblies of different generations together with the main functional groups at 2250 cm^{-1} featuring C≡N stretching, 3469 cm^{-1} (–NH_2), 3390 cm^{-1} featuring the –OH group, and other supporting spectra (data given). The primary amine was clearly observed in Generation 1.0 and overlapped with the hydroxyl group in Generation 2.0. Thus, assuring the presence of the hydroxyl group even after Michael addition reaction avoided the possibility of side reactions of the focal point during the functionalisation of branches.

^{1}H-NMR

The progress of generation advancement was followed by NMR spectroscopy with the increase in the branching of PEaDron wedges. In the ^{1}H-NMR spectra, resonance ranged from 2.0 ppm to 4.0 ppm. PEaDron G0.5 integration ratio of the peaks a:b:c:d was almost the same as 1:1:2:2, indicating that two nitrile groups attached onto ethanolamine. All peaks were triplets of protons at 3.65 (CH_2–OH), 2.74 (CH_2–N), 2.94 and 2.62 ppm (CH_2–CN). In Generation 1.0, the peaks were still clearly observed, and only grouping integration could integrate the protons according to their environment. Nevertheless, the methylene proton next to the nitrile group shifted from 2.62 ppm to 2.43 ppm. The conversion was further confirmed by ^{13}C-NMR, specifically the appearance of the nitrile group at ~120 ppm (PEaDron G0.5 and 1.5) which will be explained in the next section. For higher generations, some signals could not be distinguished due to the overlapping of different generations. Multiplets were formed and integrated accordingly by their methylene group, as referenced with 3.82 ppm (CH_2–OH), 3.78–3.65 (CH_2–N near hydroxyl group, CH_2CH_2–N), 2.51–2.30 (CH_2–N near nitrile group), and 2.94–2.60 (CH_2–CN). All spectral data were in agreement with the proposed structure.

^{13}C-NMR

Both ^{13}C solid and liquid NMR were used to identify the changes at the peripheral sites of the dendron as a result of increasing generation. Generation 0.5, the only liquid product was identified using deuterium oxide on ^{13}C liquid NMR. Several signals were observed at 18.2 ppm (–CH_2–CN–), 33.4 ppm (–CH_2–CH_2–), 49.5ppm and 54.4ppm (–CH_2–N–), 60.7ppm (–CH_2–OH), and 120 ppm which was attributed to (–C≡N). The rest of the products were white solids and thus they were examined using ^{13}C solid NMR. In Generation 1.0, signals at 34.9 ppm (–CH_2–N–), 46.6 ppm (–CH_2–CH_2–N–), 50.7 ppm (–CH_2–NH_2–), 55.3 ppm (–CH_2–CH_2–NH_2–), and 59.4 ppm (N–CH_2–CH_2–OH) represented the resonance of the corresponding functional groups [55]. The results were similar to those of the synthesised poly(propyleneimine) dendrimers reported by Brabender-Van Den Berg and Meijer [55] except that there was consistent appearance of hydroxyl groups throughout the generations which indicated that no reaction occurred at this side of functional group.

Resonance bands for G1.5 were 17.2 ppm (–CH_2–CN–), 19.0 ppm (–CH_2–CH_2–CN), 33.9 ppm (–CH_2–N–), 36.2 ppm (–CH_2–CH_2–N–), 39.1 ppm (N–CH_2–CH_2–N–), 49.4 ppm (N–CH_2–CH_2–CN), 58.7ppm (–CH_2–OH), 59.8ppm (N–CH_2–CH_2–OH), and 121.5 ppm which was attributed to (–C≡N). While the bands for G2.0 were 22.4 ppm (N–CH_2–CH_2–N–), 30.3 ppm (–CH_2–CH_2–NH_2–), 39.4 ppm (–CH_2–NH_2–), 49.7 ppm (N–CH_2–CH_2–NH_2–), 58.9 ppm (N–CH_2–CH_2–OH), and 67.2 ppm (–CH_2–N–CH_2–CH_2).

Through the NMR spectroscopy, the defective structures or incompletely reduced dendrons could be identified. The emergence of carbonyl group resonance of ester functionality at 164.8 ppm in G1.0 was the result of complete nitrile reduction of nitrile to amine following hydrolysis of nitrile to amide intermediate. The addition signals in the ^{13}C solid NMR were easily identified at 169.9 and 177 ppm in G2.0 as the by-products due to side reaction with water forming secondary amine. Formation of aldehyde was due to nucleophilic attack on cyano carbon since the nucleophiles (water) could also attack the nitrile group [56]. The carryover of previous generations was seen in Generations 1.0 to 2.0, however the main generation data were still consistent with the proposed dendron structures with the characterisation of other instrument. Detailed resonance bands are shown in Figure 4.

MALDI–ToF

Matrix-assisted laser desorption-ionization-time of flight mass spectrometry (MALDI-TOF-MS) was collected on TOF/TOFTM 5800 system (Ab Sciex, Framingham, MA) equipped with 1 kHz laser, providing lightning-fast ionization and highest–confidence of identification with fewest number of laser shots. It can be used to determine organic compounds of low molecular weight starting from a mass of 200 (Generations 1.5 and 2.0). Due to the hygroscopic nature of alcohol and amine terminated dendrimers, their elemental analyses were not easily detectable [10]. However, by having charged compensation and followed by ionisation, they can be detected as singly charged ions and forming adducts with Na^+, H^+, and K^+. Both analyses were carried out using α–Cyano–4–hydroxycinnamic acid (CHCA) as matrix, as this peak does not interfere with peaks arising from analytes nor causes fragmentation reactions.

The mass spectra of Generations 1.5 and 2.0 PEaDron were secured and the elemental composition analyses were performed on both nitrile and amine functional groups. MALDI–TOF spectra are represented in Figure 5, with their peaks labelled according to their *m/z* ratio. The obtained molar mass corresponded very well with the expected theoretical mass. PEaDron G1.5 synthesis was ascertained of its completeness of synthetic route with isotopic multiplets centred at *m/z* 304.2 $[M + H^+]^+$ (Calc. 304.3) and *m/z* 326.3 $[M + Na^+]^+$ (Calc. 326.3) corresponding to the alkali adduct. Trace signals attributable to incomplete Michael additions were detectable at *m/z* 318.3, 316.4, and 311.0. After synthesis of PEaDron Generation 0.5, remainder of acrylonitrile which did not take part in Michael additions was reduced by

Raney nickel to allyamine in Generation 1.0 as well as side products of retro– Michael additions of dendrimers with NH_2 end groups [39], causing confusing peripheral sites construction in Generation 1.5. These led to the additions of impurities and defects which however were insignificant.

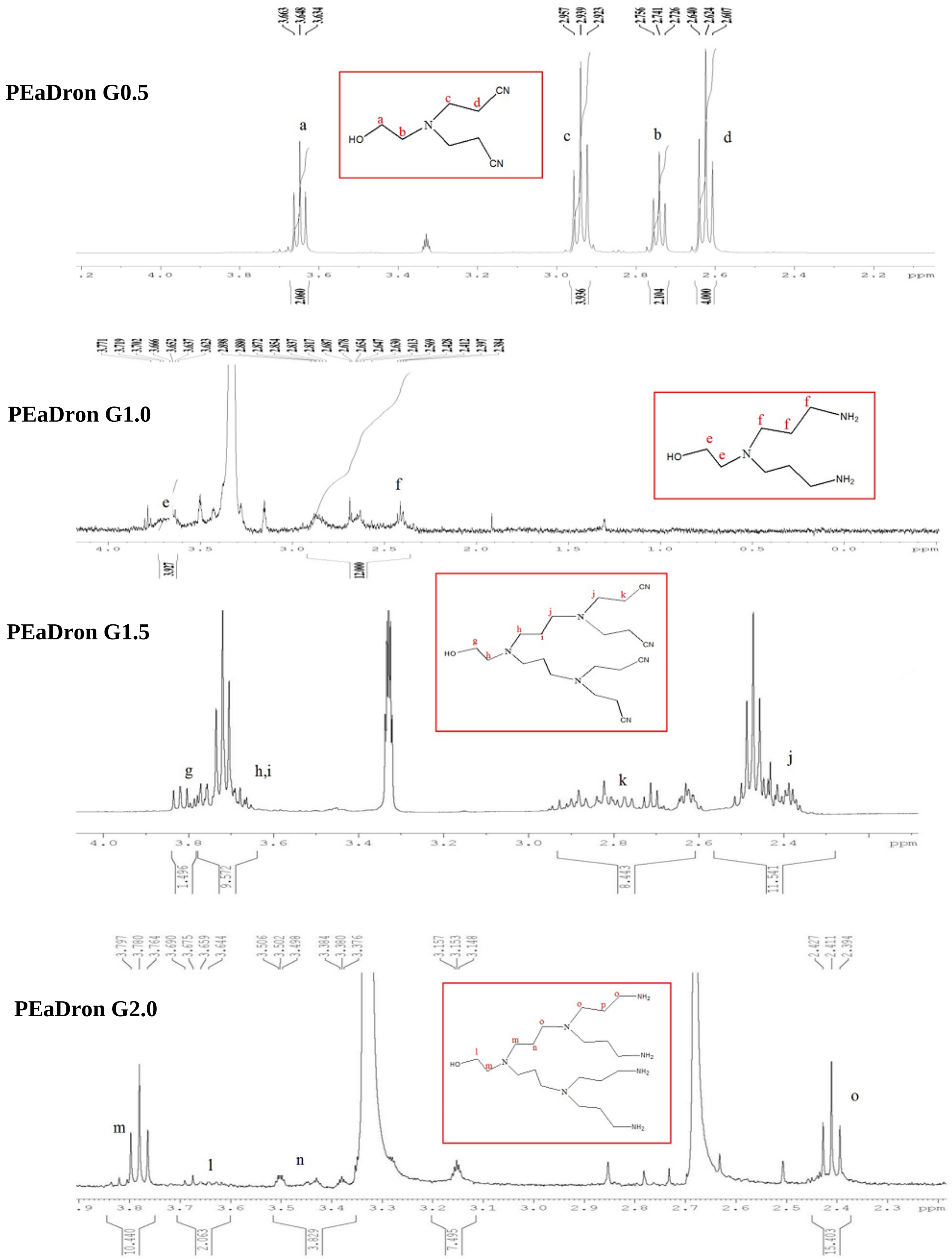
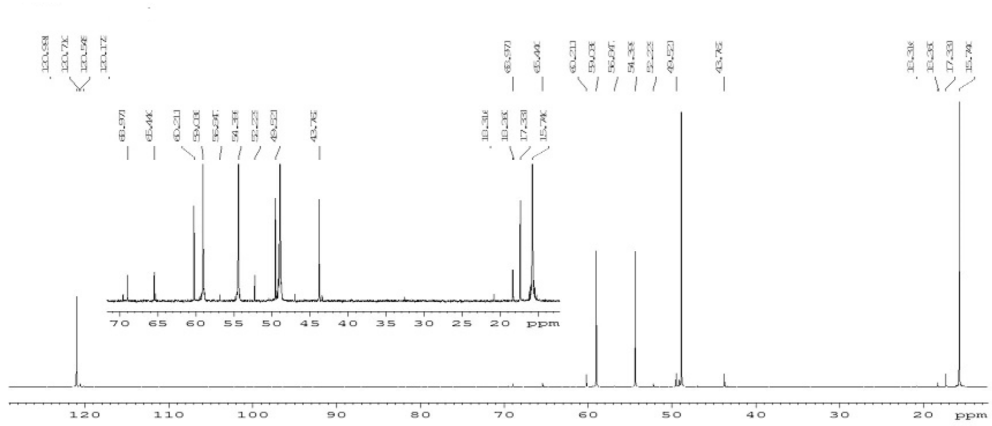
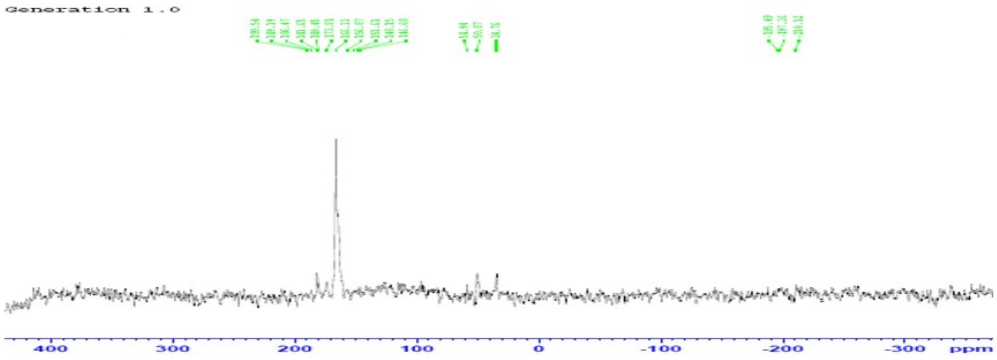
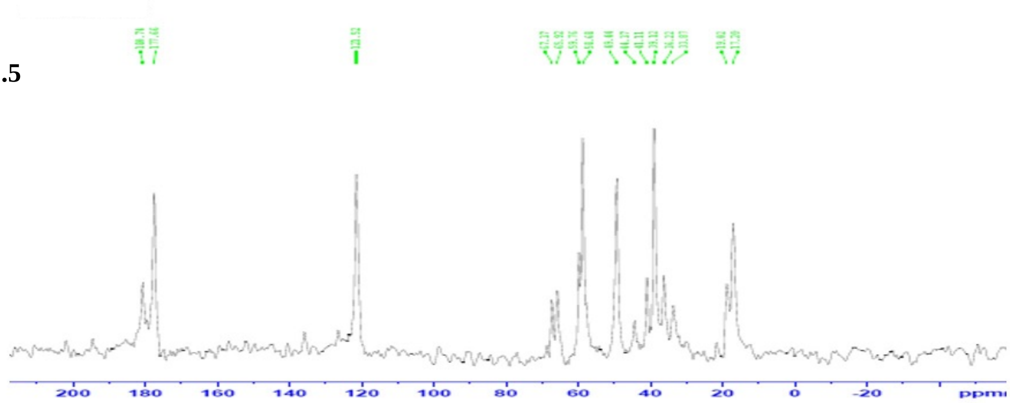


Figure 3. ^{1}H–NMR spectra of PEaDron at different generations of PEaDron Generation 0.5 to Generation 2.0.


PEaDron G0.5


PEaDron G1.0


PEaDron G1.5

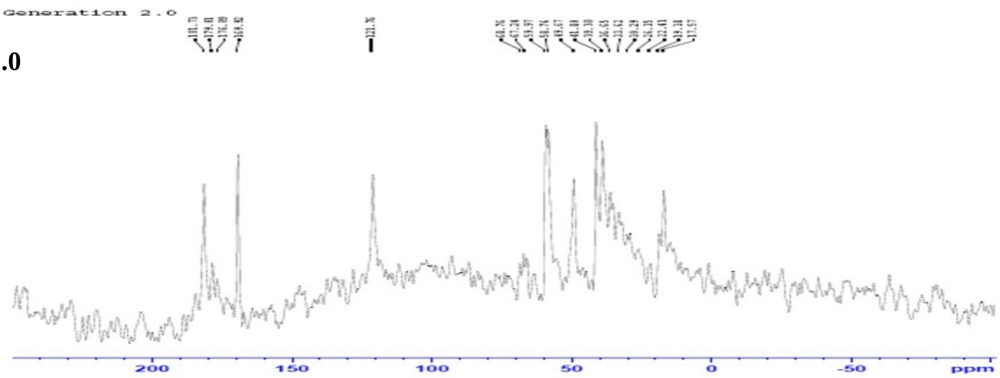

PEaDron G2.0

Figure 4. ^{13}C–NMR spectra of PEaDron at different generations of PEaDron Generation 0.5 to Generation 2.0.

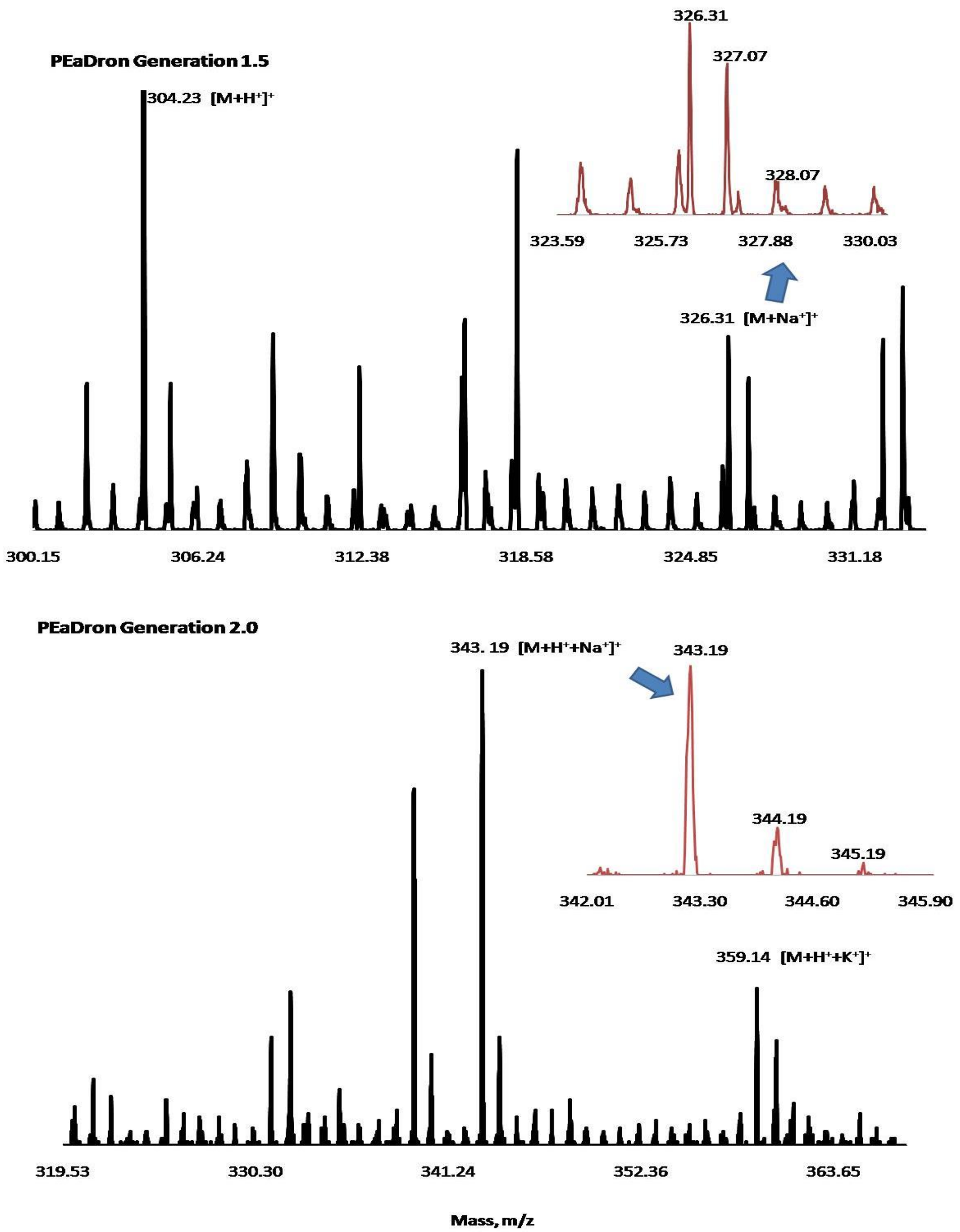


Figure 5. MALDI–TOF mass spectra of G1.5–CN and G2.0–NH_2, Matrix: CHCA.

Reduction of nitriles in Generation 2.0 was successful where the purity of the product was supported by MALDI–TOF mass spectrum, which substantiated the molecule of mass at m/z 343.2 [M + H+ + Na+]+ (Calc. 343.5) and m/z 359.1 [M + H+ + K+]+ (Calc. 359.1). In addition, peaks with the presence of loop defects were detected at m/z 332.3 and 339.3. Due to its "polymeric nature" by divergent approach, all listed defects were the results of accumulation of the previous generations and also as continuation of being molecular fragments in the upcoming generations.

CONCLUSION

PEaDron up to Generation 2.0, which presented a hydroxyl focal point and amine peripheral functionality, was successfully synthesised. This new material was confirmed through analysis via IR, ^{1}H-NMR, ^{13}C-NMR, and Maldi-Tof. The facile methodology, high yield, and easy characterisation make it interesting for further investigations. All generations were readily soluble in water but partially in methanol and ethanol. These dendrons provide possibilities of other application studies for photo-responsive studies, metal-ion detectors and extractors, pharmacology analysis, and wastewater treatment.

ACKNOWLEDGEMENT

The authors would like to thank Universiti Teknologi Malaysia (UTM) for facilitations and Ministry of Science and Technology and Innovation, Malaysia (MOSTI) for financial supports through Research Grant No. R.J130000.7909.4S069 and studentship for M.H. Chong.

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